

- <110> Tamburini, Paul P
 Davis, Gary
 Delaria, Katherine A
 Christopher, Marlor W
 Daniel, Muller K
- <120> Human Bikunin
- <130> 96-223-ZZ
- <140> US 09/974,026
- <141> 2001-10-10
- <150> US 09/144,428
- <151> 1998-08-31
- <150> PCT/US97/03894
- <151> 1997-03-10
- <150> US 08/725,251
- <151> 1996-10-04
- <150> US 60/019,793
- <151> 1996-06-14
- <150> US 60/013,106
- <151> 1996-03-11
- <160> 105
- <170> PatentIn version 3.1
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- <213> Homo sapiens
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- Val Gly Arg Cys Arg Ala Ser Met Pro Arg Trp Trp Tyr Asn Val Thr
 20 25 30
- Asp Gly Ser Cys Gln Leu Phe Val Tyr Gly Gly Cys Asp Gly Asn Ser 35 40
- Asn Asn Tyr Leu Thr Lys Glu Glu Cys Leu Lys Lys Cys Ala Thr Val 50 55 60

Thr Glu Asn Ala Thr Gly Asp Leu Ala Thr Ser Arg Asn Ala Ala Asp

Ser Ser Val Pro Ser Ala Pro Arg Arg Gln Asp Ser Glu Asp His Ser

Ser Asp Met Phe Asn Tyr Glu Glu Tyr Cys Thr Ala Asn Ala Val Thr 100 105

Gly Pro Cys Arg Ala Ser Phe Pro Arg Trp Tyr Phe Asp Val Glu Arg 120

Asn Ser Cys Asn Asn Phe Ile Tyr Gly Gly Cys Arg Gly Asn Lys Asn 135

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Val Thr Asp Gly Ser Cys Gln Leu Phe Val Tyr Gly Gly Cys Asp Gly 50 55 60

Asn Ser Asn Asn Tyr Leu Thr Lys Glu Glu Cys Leu Lys Lys Cys Ala 70 75 80

Thr Val Thr Glu Asn Ala Thr Gly Asp Leu Ala Thr Ser Arg Asn Ala 85 90 95

Ala Asp Ser Ser Val Pro Ser Ala Pro Arg Arg Gln Asp Ser Glu Asp 100 105 110

His Ser Ser Asp Met Phe Asn Tyr Glu Glu Tyr Cys Thr Ala Asn Ala 115 120 125

Val Thr Gly Pro Cys Arg Ala Ser Phe Pro Arg Trp Tyr Phe Asp Val 130 135 140

Glu Arg Asn Ser Cys Asn Asn Phe Ile Tyr Gly Gly Cys Arg Gly Asn 145 150 155 160

Lys Asn Ser Tyr Arg Ser Glu Glu Ala Cys Met Leu Arg Cys Phe Arg 165 170 175

Gln Gln Glu Asn Pro Pro Leu Pro Leu Gly Ser Lys Val Val Leu 180 185 190

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Phe Val Tyr Gly Gly Cys Asp Gly Asn Ser Asn Asn Tyr Leu Thr Lys 35 40 45

Glu Glu Cys Leu Lys Lys Cys Ala Thr Val Thr Glu Asn Ala Thr Gly

Asp Leu Ala Thr Ser Arg Asn Ala Ala Asp Ser Ser Val Pro Ser Ala

Pro Arg Arg Gln Asp Ser Glu Asp His Ser Ser Asp Met Phe Asn Tyr

Glu Glu Tyr Cys Thr Ala Asn Ala Val Thr Gly Pro Cys Arg Ala Ser 105

Phe Pro Arg Trp Tyr Phe Asp Val Glu Arg Asn Ser Cys Asn Asn Phe 115 120 125

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Glu Glu Cys Leu Lys Lys Cys Ala Thr Val 55

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Lys Lys Cys 50

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Glu Ala Cys Met Leu Arg Cys Phe Arg Gln 50 55

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20 25 30

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Lys Val Val Gly Arg Cys Arg Ala Ser Met Pro Arg Trp Trp Tyr Asn 35 40 45

Val Thr Asp Gly Ser Cys Gln Leu Phe Val Tyr Gly Gly Cys Asp Gly 50 55 60

Asn Ser Asn Asn Tyr Leu Thr Lys Glu Glu Cys Leu Lys Lys Cys Ala 65 70 75 80

Thr Val Thr Glu Asn Ala Thr Gly Asp Leu Ala Thr Ser Arg Asn Ala 85 90 95

Ala Asp Ser Ser Val Pro Ser Ala Pro Arg Arg Gln Asp Ser Glu Asp 100 105 110

His Ser Ser Asp Met Phe Asn Tyr Glu Glu Tyr Cys Thr Ala Asn Ala 115 120 125

Val Thr Gly Pro Cys Arg Ala Ser Phe Pro Arg Trp Tyr Phe Asp Val 130 135 140

Glu Arg Asn Ser Cys Asn Asn Phe Ile Tyr Gly Gly Cys Arg Gly Asn 145 150 155 160

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- Xaa Gly Xaa Cys Xaa Xaa Xaa Xaa Xaa Xaa Trp Trp Tyr Asn Val Thr 20 25 30
- Asp Gly Ser Cys Gln Leu Phe Xaa Tyr Xaa Gly Cys Xaa Xaa Xaa Ser 35 40 45
- Asn Asn Tyr Xaa Thr Lys Glu Glu Cys Leu Lys Lys Cys Ala Thr Xaa 50 55 60
- Thr Glu Asn Ala Thr Gly Asp Leu Ser Thr Ser Arg Asn Ala Ala Asp
 65 70 75 80
- Ser Ser Val Pro Ser Ala Pro Arg Arg Gln Asp Ser Glu His Asp Ser 85 90 95

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            100
Gly Xaa Cys Xaa Xaa Xaa Xaa Xaa Trp Tyr Phe Asp Val Glu Arg
        115
Asn Ser Cys Asn Asn Phe Xaa Tyr Xaa Gly Cys Xaa Xaa Xaa Lys Asn
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Ser Tyr Xaa Ser Glu Glu Ala Cys Met Leu Arg Cys Phe Arg Xaa Gln
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Ala Val Ser
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Lys Val Val Gly Arg Glu Arg Ala Ser Met Pro Arg Trp Trp Tyr Asn 35 40 45

Val Thr Asp Gly Ser Cys Gln Leu Phe Val Tyr Gly Gly Cys Asp Gly 50 55 60

Asn Ser Asn Asn Tyr Leu Thr Lys Glu Glu Cys Leu Lys Lys Cys Ala 65 70 75 80

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<223> "n" is any nucleotide.
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                                                                       120
aaggcaggat totgaagaco actocagoga tatgttcaac tatgaagaat actgcacogo
                                                                       180
caacgcagtc actgggcctt gccgtgcatc cttcccacgc tggtactttg acgtggagag
                                                                       240
                                                                       300
gaactcctgc aataacttca tctatggagg ctgccggggc aataagaaca gctaccgctc
tgaggaggcc tgcatgctcc gctgcttccg ccagcaggag aatcctcccc tgccccttgg
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ctcaaaggtg gtggttctgg ccggggctgt ttcgtgatgg tgttgatcct tttcctgggg
                                                                       420
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Glu Cys His Gly
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<210> 16 <211> 428

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catgcctagg tggtggtaca atgtcactga cggatcctgc cagctgtttg tgtatggggg
                                                                    180
ctgtgacgga aacagcaata attacctgac caaggaggag tgcctcaaga aatgtgccac
                                                                    240
tgtcacagag aatgccacgg gtgacctggc caccagcagg aatgcagcgg attcctctgt
                                                                    300
cccaagtgct cccagaaggc aggattctga agaccactcc agcgatatgt tcaactatga
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<223> "n" is any nucleotide.
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caatgtcact gacggatcct gccagctgtt tgtgtatggg ggctgtgacg gaaacagcaa
taattacctg accaaggagg agtgcctcaa gaaatgtgcc actgtcacag agaatgccac
gggtgacctg gccaccagca ggaatgcagc ggattcctct gtcccaagtg ctcccagaag
                                                                         300
gcaggattct gaagaccact ccagcgatat gttcaactat gaagaatact gcaccgccaa
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Met Lys Arg Phe Phe Phe Asn Ile Phe Thr Arg Gln Cys Glu Glu Phe
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Ile Tyr Gly Gly Cys Glu Gly Asn Gln Asn Arg Phe Glu Ser Leu Glu

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Lys Tyr Gly Gly Cys Leu Gly Asn Met Asn Asn Phe Glu Thr Leu Glu
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Glu Cys Lys Asn Ile Cys Glu Asp Gly
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<223> Kunitz-like domain of tissue factor pathway inhibitor precursor.
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Glu Asn Arg Phe Tyr Tyr Asn Ser Val Ile Gly Lys Cys Arg Pro Phe
Lys Tyr Ser Gly Cys Gly Gly Asn Glu Asn Asn Phe Thr Ser Lys Gln
Glu Cys Leu Arg Ala Cys Lys Lys Gly
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Glu Cys Lys Lys Met Cys Thr Arg Asp

<210> 21

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Leu Tyr Gly Gly Cys Glu Gly Asn Ala Asn Asn Phe Tyr Thr Trp Glu

Ala Cys Asp Asp Ala Cys Trp Arg Ile

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<213> Unknown

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<223> Kunitz-like domain of tissue factor pathway inhibitor precursor 2.

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Val Thr Arg Tyr Tyr Phe Asn Pro Arg Tyr Arg Thr Cys Asp Ala Phe

Thr Tyr Thr Gly Cys Gly Asn Asn Asp Asn Asn Phe Val Ser Arg Glu

Asp Ser Lys Arg Ala Cys Ala Lys Ala

<210> 23

<211> 57

<212> PRT

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<223> Kunitz-like domain of amyloid precursor protein homologue.

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Met Pro Arg Thr Thr Phe Asp Leu Ser Lys Gly Lys Cys Val Arg Phe 20 25 30

Ile Thr Gly Gly Cys Gly Gly Asn Arg Asn Asn Phe Glu Ser Glu Asp 35 40 45

Tyr Cys Met Ala Val Cys Lys Ala Met 50 55

<210> 24

<211> 58

<212> PRT

<213> Unknown

<220>

<223> Kunitz-like domain of aprotinin.

<400> 24

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Arg Ile Ile Arg Tyr Phe Tyr Asn Ala Lys Ala Gly Leu Cys Gln Thr 20 25 30

Phe Val Tyr Gly Gly Cys Arg Ala Lys Arg Asn Asn Phe Lys Ser Ala 35 40 45

Glu Asp Cys Met Arg Thr Cys Gly Gly Ala 50 55

<210> 25

<211> 51

<212> PRT

<213> Unknown

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<223> Kunitz-like domain of inter-alpha-trypsin inhibitor precursor.

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Cys Gln Leu Gly Tyr Ser Ala Gly Pro Cys Met Gly Met Thr Ser Arg

10 5 15 1

Tyr Phe Tyr Asn Gly Thr Ser Met Ala Cys Glu Thr Phe Gln Tyr Gly 20 25

Gly Cys Met Gly Asn Gly Asn Asn Phe Val Thr Glu Lys Glu Cys Leu 40

Gln Thr Cys 50

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<223> Kunitz-like domain of inter-alpha-trypsin inhibitor precursor.

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Val Ala Ala Cys Asn Leu Pro Ile Val Arg Gly Pro Cys Arg Ala Phe

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Pro Tyr Gly Gly Cys Gln Gly Asn Gly Asn Lys Phe Tyr Ser Glu Lys

Glu Cys Arg Glu Tyr Cys Gly Val Pro

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<213> Unknown

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<223> Kunitz-like domain of amyloid precursor protein.

<400> 27

Glu Val Cys Cys Ser Glu Gln Ala Glu Thr Gly Pro Cys Arg Ala Met

Ile Ser Arg Trp Tyr Phe Asp Val Thr Glu Gly Lys Cys Ala Pro Phe 25

Phe Tyr Gly Gly Cys Gly Gly Asn Arg Asn Asn Phe Asp Thr Glu Glu 35 40 45

Tyr Cys Met Ala Val Cys Gly Ser Ala 50 55

<210> 28

<211> 51

<212> PRT

<213> Unknown

<220>

<223> Kunitz-like domain of collagen alpha-3(VI) precursor.

<400> 28

Cys Lys Leu Pro Lys Asp Glu Gly Thr Cys Arg Asp Phe Ile Leu Lys 1 $$ 5 $$ 10 $$ 15

Trp Tyr Tyr Asp Pro Asn Thr Lys Ser Cys Ala Arg Phe Trp Tyr Gly 20 25 30

Gly Cys Gly Gly Asn Glu Asn Lys Phe Gly Ser Gln Lys Glu Cys Glu 35 40 45

Lys Val Cys 50

<210> 29

<211> 57

<212> PRT

<213> Unknown

<220>

<223> Kunitz-like domain of HKI-B9.

<400> 29

Met Thr Arg Trp Phe Phe Asn Phe Glu Thr Gly Glu Cys Glu Leu Phe 20 25 30

Ala Tyr Gly Gly Cys Gly Gly Asn Ser Asn Asn Phe Leu Arg Lys Glu 35 40 45

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Lys Cys Glu Lys Phe Cys Lys Phe Thr
   50
<210> 30
<211> 46
<212> DNA
<213> Artificial Sequence
<220>
<223> 5' sense oligonucleotide used in Example 6.
<400> 30
gccaagcttg gataaaagat atgaagaata ctgcaccgcc aacgca
                                                                     46
<210> 31
<211> 35
<212> DNA
<213> Artificial Sequence
<220>
<223> 3' antisense oligonucleotide used in Example 6.
<400> 31
                                                                     35
ggggatcctc actgctggcg gaagcagcgg agcat
<210> 32
<211> 206
<212> DNA
<213> Artificial Sequence
<220>
<223> Cloned bikunin cDNA fragment in Example 6.
<400> 32
ccaagettgg ataaaagata tgaagaatac tgcaccgcca acgcagtcac tgggcettgc
                                                                     60
cgtgcatcct tcccacgctg gtactttgac gtggagagga actcctgcaa taacttcatc
                                                                    120
tatggaggct gccggggcaa taagaacagc taccgctctg aggaggcctg catgctccgc
                                                                    180
tgcttccgcc agcagtgagg atcccc
                                                                    206
<210> 33
<211> 28
<212> DNA
<213> Artificial Sequence
<220>
<223> 3' PCR primer used to amplify EST R74593.
<400> 33
                                                                     28
cgaagcttca tctccgaagc tccagacg
```

```
<210> 34
<211> 31
<212> DNA
<213> Artificial Sequence
<220>
<223> 5' PCR primer used to amplify EST R74593.
<400> 34
                                                                      31
aggatctaga caataattac ctgaccaagg a
<210> 35
<211>
      37
<212> DNA
<213> Artificial Sequence
<220>
<223> 5' PCR primer used to amplify EST R35464.
<400> 35
                                                                       37
ggtctagagg ccgggtccgt ttctcgcctg gctggga
<210> 36
 <211> 19
 <212> DNA
 <213> Artificial Sequence
 <220>
 <223> 5' PCR primer used to amplify EST R34808.
 <400> 36
                                                                       19
 cacctgatcg cgagacccc
 <210> 37
 <211> 19
 <212> DNA
<213> Artificial Sequence
 <220>
 <223> Vector specific DNA sequencing primer (SP6).
 <400> 37
                                                                       19
 gatttaggtg acactatag
 <210> 38
 <211> 20
 <212> DNA
 <213> Artificial Sequence
 <220>
 <223> Vector specific DNA sequencing primer (T7).
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| <400> | 38 | |
|---------------|---|-----|
| taatac | gact cactataggg | 20 |
| | | |
| | | |
| <210> | 39 | |
| <211> | 22 | |
| | | |
| <212> | | |
| <213> | Artificial Sequence | |
| | | |
| <220> | | |
| <223> | Gene specific DNA sequencing primer. | |
| 10007 | done profit in polymer. | |
| 400 | 20 | |
| <400> | 39 | |
| ttaccto | gacc aaggaggagt gc | 22 |
| | | |
| | | |
| <210> | 40 | |
| | | |
| | 23 | |
| <212> | | |
| <213> | Artificial Sequence | |
| | | |
| <220> | | |
| <223> | Gene specific DNA sequencing primer. | |
| \223 / | dene specific bus sequencing primer. | |
| | | |
| <400> | 40 | |
| aatccg | ctgc attcctgctg gtg | 23 |
| | | |
| | | |
| <210> | 41 | |
| | | |
| <211> | 20 | |
| <212> | DNA | |
| <213> | Artificial Sequence | |
| | | |
| <220> | | |
| <223> | Gene specific DNA sequencing primer. | |
| (2237 | dene specific bux sequencing primer. | |
| | | |
| <400> | 41 | |
| cagtcad | etgg geettgeegt | 20 |
| | | |
| | | |
| .010. | 43 | |
| <210> | 42 | |
| <211> | 105 | |
| <212> | DNA | |
| <213> | Artificial Sequence | |
| | - | |
| <220> | | |
| | et a constitue and an example e | |
| <223> | 5' sense oligonucleotide used in Example 5. | |
| | | |
| <400> | 42 | |
| gaaggg | gtaa gettggataa aagatatgaa gaataetgea eegeeaaege agteaetggg | 60 |
| | | |
| ccttac | cgtg catcettece acgetggtae tttgaegtgg agagg | 105 |
| cccigc | | -00 |
| | | |
| | | |
| <210> | 43 | |
| <211> | 129 | |

| | DNA Artificial Sequence | |
|----------------|---|-----|
| <220> <223> | 3' antisense oligonucleotide used in Example 5. | |
| | 43 ccc tactggcgga agcagcggag catgcaggcc tcctcagagc ggtagctgtt | 60 |
| cttattg | ccc cggcagcctc catagatgaa gttattgcag gagttcctct ccacgtcaaa 1 | L20 |
| gtaccag | rcg 1 | 129 |
| <211> <212> | 44 207 DNA Artificial Sequence | |
| <220> <223> | Cloned bikunin fragment in Example 5. | |
| | 44 taa gettggataa aagatatgaa gaataetgea eegeeaaege agteaetggg | 60 |
| ccttgcc | gtg cateetteee aegetggtae tttgaegtgg agaggaaete etgeaataae | 120 |
| ttcatct | atg gaggetgeeg gggeaataag aacagetace getetgagga ggeetgeatg | 180 |
| ctccgct | gct teegeeagta gggatee 2 | 207 |
| <211> <212> | 45 248 PRT Artificial Sequence | |
| <220> <223> | EST derived consensus sequence of human Bikunin (Figs. 4D and 4 | 1G) |
| | SIGNAL (1)(23) | |
| <400> | 45 | |
| Met Leu 1 | Arg Ala Glu Ala Asp Gly Val Ser Arg Leu Leu Gly Ser Leu 5 10 15 | |
| Leu Leu | Ser Gly Val Leu Ala Ala Asp Arg Glu Arg Ser Ile His Asp 20 25 30 | |

Phe Cys Leu Val Ser Lys Val Val Gly Arg Cys Arg Ala Ser Met Pro

35 40 45

Arg Trp Trp Tyr Asn Val Thr Asp Gly Ser Cys Gln Leu Phe Val Tyr 50 55 60

Gly Gly Cys Asp Gly Asn Ser Asn Asn Tyr Leu Thr Lys Glu Glu Cys 70 75 80

Leu Lys Lys Cys Ala Thr Val Thr Glu Asn Ala Thr Gly Asp Leu Ala 85 90 95

Thr Ser Arg Asn Ala Ala Asp Ser Ser Val Pro Ser Ala Pro Arg Arg 100 105 110

Gln Asp Ser Glu Asp His Ser Ser Asp Met Phe Asn Tyr Glu Glu Tyr
115 120 125

Cys Thr Ala Asn Ala Val Thr Gly Pro Cys Arg Ala Ser Phe Pro Arg 130 135 140

Trp Tyr Phe Asp Val Glu Arg Asn Ser Cys Asn Asn Phe Ile Tyr Gly 145 150 155 160

Gly Cys Arg Gly Asn Lys Asn Ser Tyr Arg Ser Glu Glu Ala Cys Met 165 170 175

Leu Arg Cys Phe Arg Gln Gln Glu Asn Pro Pro Leu Pro Leu Gly Ser 180

Lys Val Val Leu Ala Gly Leu Phe Val Met Val Leu Ile Leu Phe 195 200 205

Leu Gly Ala Ser Met Val Tyr Leu Ile Arg Val Ala Arg Arg Asn Gln 210 215 220

Glu Arg Ala Leu Arg Thr Val Trp Ser Ser Gly Asp Asp Lys Glu Gln 225 230 235 240

Leu Val Lys Asn Thr Tyr Val Leu 245

<210> 46 <211> 782

| <212> DNA <213> Homo sapiens | |
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| <220> <221> exon <222> (61)(780) <223> | |
| <400> 46 acctgatcgc gagaccccaa cggctggtgg cgtcgcctgc gcgtctcggc tgagctggcc | 60 |
| atg gcg cag ctg tgc ggg ctg agg cgg agc cgg gcg ttt ctc gcc ctg Met Ala Gln Leu Cys Gly Leu Arg Arg Ser Arg Ala Phe Leu Ala Leu 1 5 10 15 | .08 |
| ctg gga tcg ctg ctc ctc tct ggg gtc ctg gcg gcc gac cga gaa cgc 1 Leu Gly Ser Leu Leu Ser Gly Val Leu Ala Ala Asp Arg Glu Arg 20 25 30 | .56 |
| agc atc cac gac ttc tgc ctg gtg tcg aag gtg gtg ggc aga tgc cgg 2 Ser Ile His Asp Phe Cys Leu Val Ser Lys Val Val Gly Arg Cys Arg 35 40 45 | 04 |
| gcc tcc atg cct agg tgg tgg tac aat gtc act gac gga tcc tgc cag Ala Ser Met Pro Arg Trp Trp Tyr Asn Val Thr Asp Gly Ser Cys Gln 50 55 60 | 252 |
| ctg ttt gtg tat ggg ggc tgt gac gga aac agc aat aat tac ctg acc Leu Phe Val Tyr Gly Gly Cys Asp Gly Asn Ser Asn Asn Tyr Leu Thr 70 75 80 | 00 |
| aag gag gag tgc ctc aag aaa tgt gcc act gtc aca gag aat gcc acg Lys Glu Glu Cys Leu Lys Lys Cys Ala Thr Val Thr Glu Asn Ala Thr 85 90 95 | 348 |
| ggt gac ctg gcc acc agc agg aat gca gcg gat tcc tct gtc cca agt Gly Asp Leu Ala Thr Ser Arg Asn Ala Ala Asp Ser Ser Val Pro Ser 100 105 110 | 96 |
| gct ccc aga agg cag gat tct gaa gac cac tcc agc gat atg ttc aac Ala Pro Arg Arg Gln Asp Ser Glu Asp His Ser Ser Asp Met Phe Asn 115 120 125 | 44 |
| tat gaa gaa tac tgc acc gcc aac gca gtc act ggg cct tgc cgt gca Tyr Glu Glu Tyr Cys Thr Ala Asn Ala Val Thr Gly Pro Cys Arg Ala 130 135 140 | 92 |
| tcc ttc cca cgc tgg tac ttt gac gtg gag agg aac tcc tgc aat aac Ser Phe Pro Arg Trp Tyr Phe Asp Val Glu Arg Asn Ser Cys Asn Asn 145 150 155 160 | 540 |
| ttc atc tat gga ggc tgc cgg ggc aat aag aac agc tac cgc tct gag Phe Ile Tyr Gly Gly Cys Arg Gly Asn Lys Asn Ser Tyr Arg Ser Glu 165 170 175 | 88 |
| gag gcc tgc atg ctc cgc tgc ttc cgc cag cag gag aat cct ccc ctg 6 | 536 |

| 180 185 190 |
|---|
| ccc ctt ggc tca aag gtg gtg gtt ctg gcg ggg ctg ttc gtg atg gtg Pro Leu Gly Ser Lys Val Val Val Leu Ala Gly Leu Phe Val Met Val 195 200 205 |
| ttg atc ctc ttc ctg gga gcc tcc atg gtc tac ctg atc cgg gtg gca Leu Ile Leu Phe Leu Gly Ala Ser Met Val Tyr Leu Ile Arg Val Ala 210 215 220 |
| cgg agg aac cag gag cgt gcc ctg cgc acc gtc tgg agc ttc gga gat Arg Arg Asn Gln Glu Arg Ala Leu Arg Thr Val Trp Ser Phe Gly Asp 235 230 235 240 |
| ga 782 |
| <210> 47 <211> 240 <212> PRT <213> Homo sapiens |
| <220> <221> SIGNAL <222> (1)(27) <223> |
| <400> 47 |
| |
| Met Ala Gln Leu Cys Gly Leu Arg Arg Ser Arg Ala Phe Leu Ala Leu 1 5 10 15 |
| Met Ala Gln Leu Cys Gly Leu Arg Arg Ser Arg Ala Phe Leu Ala Leu |
| Met Ala Gln Leu Cys Gly Leu Arg Arg Ser Arg Ala Phe Leu Ala Leu 1 5 10 15 Leu Gly Ser Leu Leu Leu Ser Gly Val Leu Ala Ala Asp Arg Glu Arg |
| Met Ala Gln Leu Cys Gly Leu Arg Arg Ser Arg Ala Phe Leu Ala Leu 15 Leu Gly Ser Leu Leu Leu Ser Gly Val Leu Ala Ala Asp Arg Glu Arg 25 Ser Ile His Asp Phe Cys Leu Val Ser Lys Val Val Gly Arg Cys Arg |
| Met Ala Gln Leu Cys Gly Leu Arg Arg Ser Arg Ala Phe Leu Ala Leu 15 Leu Gly Ser Leu Leu Leu Ser Gly Val Leu Ala Ala Asp Arg Glu Arg 25 Ser Ile His Asp Phe Cys Leu Val Ser Lys Val Val Gly Arg Cys Arg 40 Ala Ser Met Pro Arg Trp Trp Tyr Asn Val Thr Asp Gly Ser Cys Gln |
| Met Ala Gln Leu Cys Gly Leu Arg Arg Ser Arg Ala Phe Leu Ala Leu 15 Leu Gly Ser Leu Leu Leu Ser Gly Val Leu Ala Ala Asp Arg Glu Arg 25 Ser Ile His Asp Phe Cys Leu Val Ser Lys Val Val Gly Arg Cys Arg 45 Ala Ser Met Pro Arg Trp Trp Tyr Asn Val Thr Asp Gly Ser Cys Gln 50 Leu Phe Val Tyr Gly Gly Cys Asp Gly Asn Ser Asn Asn Tyr Leu Thr |

115 120 Tyr Glu Glu Tyr Cys Thr Ala Asn Ala Val Thr Gly Pro Cys Arg Ala 135 140 130 Ser Phe Pro Arg Trp Tyr Phe Asp Val Glu Arg Asn Ser Cys Asn Asn 145 150 155 Phe Ile Tyr Gly Gly Cys Arg Gly Asn Lys Asn Ser Tyr Arg Ser Glu 165 170 Glu Ala Cys Met Leu Arg Cys Phe Arg Gln Gln Glu Asn Pro Pro Leu 180 185 Pro Leu Gly Ser Lys Val Val Leu Ala Gly Leu Phe Val Met Val 195 200 205 Leu Ile Leu Phe Leu Gly Ala Ser Met Val Tyr Leu Ile Arg Val Ala 210 Arg Arg Asn Gln Glu Arg Ala Leu Arg Thr Val Trp Ser Phe Gly Asp <210> 48 <211> 1544 <212> DNA <213> Homo sapiens <220> <221> misc_feature <222> (1358)..(1358) <223> "n" is any nucleotide. <220> <221> exon <222> (301)..(1056) <223> <400> 48 gcacgagttg ggaggtgtag cgcggctctg aacgcgctga gggccgttga gtgtcgcagg 60 cggcgagggc gcgagtgagg agcagaccca ggcatcgcgc gccgagaagg ccgggcgtcc 120 ccacactgaa ggtccggaaa ggcgacttcc gggggctttg gcacctggcg gaccctcccg 180

Ala Pro Arg Arg Gln Asp Ser Glu Asp His Ser Ser Asp Met Phe Asn

| gagcgtcggc acc | tgaacgc gag | cgctcc at | tgcgcgtg | cgcgttgagg g | ggcttcccgc | 240 |
|---|--------------|-----------|----------|--------------|------------|-----|
| acctgatcgc gag | accccaa cgg | tggtgg cg | tcgcctgc | gcgtctcggc | tgagctggcc | 300 |
| atg gcg cag ct Met Ala Gln Le 1 | | | | | | 348 |
| ctg gga tcg ct Leu Gly Ser Le 20 | u Leu Leu Se | | | | | 396 |
| agc atc cac ga Ser Ile His As 35 | | | | | | 444 |
| gcc tcc atg cc Ala Ser Met Pr 50 | | p Tyr Asn | | | | 492 |
| ctg ttt gtg ta Leu Phe Val Ty 65 | | | | | | 540 |
| aag gag gag tg Lys Glu Glu Cy | | | | | | 588 |
| ggt gac ctg gc Gly Asp Leu Al | a Thr Ser A | | | | | 636 |
| gct ccc aga ag Ala Pro Arg Ar 115 | | | | _ | | 684 |
| tat gaa gaa ta Tyr Glu Glu Ty 130 | | a Asn Ala | _ | | | 732 |
| tcc ttc cca cg Ser Phe Pro Ar 145 | | | | | | 780 |
| ttc atc tat go Phe Ile Tyr Gl | | | | | | 828 |
| gag gcc tgc at Glu Ala Cys Me 18 | et Leu Arg C | | | | | 876 |
| ccc ctt ggc to Pro Leu Gly Se 195 | | | | | | 924 |

| ttg atc ctc ttc ctg gga gcc tcc atg gtc tac ctg atc cgg gtg gca Leu Ile Leu Phe Leu Gly Ala Ser Met Val Tyr Leu Ile Arg Val Ala 210 215 220 | 972 |
|---|------|
| cgg agg aac cag gag cgt gcc ctg cgc acc gtc tgg agc tcc gga gat Arg Arg Asn Gln Glu Arg Ala Leu Arg Thr Val Trp Ser Ser Gly Asp 235 240 | 1020 |
| gac aag gag cag ctg gtg aag aac aca tat gtc ctg tgaccgccct Asp Lys Glu Gln Leu Val Lys Asn Thr Tyr Val Leu 245 250 | 1066 |
| gtcgccaaga ggactgggga agggagggga gactatgtgt gagctttttt taaatagagg | 1126 |
| gattgactcg gatttgagtg atcattaggg ctgaggtctg tttctctggg aggtaggacg | 1186 |
| getgetteet ggtetggeag ggatgggttt getttggaaa teetetagga ggeteeteet | 1246 |
| cgcatggcct gcagtctggc agcagccccg agttgtttcc tcgctgatcg atttctttcc | 1306 |
| tccaggtaga gttttctttg cttatgttga attccattgc ctccttttct cnatcacaga | 1366 |
| agtgatgttg gaatcgtttc ttttgtttgt ctgatttatg gtttttttaa gtataaacaa | 1426 |
| aagtttttta ttagcattct gaaagaagga aagtaaaatg tacaagttta ataaaaaggg | 1486 |
| gccttcccct ttagaataaa tttccagcat gttgctttca aaaaaaaaa aaaaaaaa | 1544 |

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<211> 252 <212> PRT

<213> Homo sapiens

<220>

<221> SIGNAL

<222> (1)..(27)

<223>

<400> 49

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Leu Gly Ser Leu Leu Ser Gly Val Leu Ala Ala Asp Arg Glu Arg 20

Ser Ile His Asp Phe Cys Leu Val Ser Lys Val Val Gly Arg Cys Arg 35 45

Ala Ser Met Pro Arg Trp Trp Tyr Asn Val Thr Asp Gly Ser Cys Gln 50 55

Leu Phe Val Tyr Gly Gly Cys Asp Gly Asn Ser Asn Asn Tyr Leu Thr 75 80

Lys Glu Glu Cys Leu Lys Lys Cys Ala Thr Val Thr Glu Asn Ala Thr 85 90 95

Gly Asp Leu Ala Thr Ser Arg Asn Ala Ala Asp Ser Ser Val Pro Ser

Ala Pro Arg Arg Gln Asp Ser Glu Asp His Ser Ser Asp Met Phe Asn 115 120 125

Tyr Glu Glu Tyr Cys Thr Ala Asn Ala Val Thr Gly Pro Cys Arg Ala 130 135 140

Ser Phe Pro Arg Trp Tyr Phe Asp Val Glu Arg Asn Ser Cys Asn Asn 145 150 150 160

Phe Ile Tyr Gly Gly Cys Arg Gly Asn Lys Asn Ser Tyr Arg Ser Glu 165 170 175

Glu Ala Cys Met Leu Arg Cys Phe Arg Gln Gln Glu Asn Pro Pro Leu 180 185 190

Pro Leu Gly Ser Lys Val Val Leu Ala Gly Leu Phe Val Met Val 195 200 205

Leu Ile Leu Phe Leu Gly Ala Ser Met Val Tyr Leu Ile Arg Val Ala 210 215 220

Arg Arg Asn Gln Glu Arg Ala Leu Arg Thr Val Trp Ser Ser Gly Asp 225 230 230 235

Asp Lys Glu Gln Leu Val Lys Asn Thr Tyr Val Leu 245 250

<210> 50

<211> 146

<212> PRT

<213> Homo sapiens

<400> 50

Cys Leu Val Ser Lys Val Val Gly Arg Cys Arg Ala Ser Met Pro Arg

Trp Trp Tyr Asn Val Thr Asp Gly Ser Cys Gln Leu Phe Val Tyr Gly 20 25 30

Gly Cys Asp Gly Asn Ser Asn Asn Tyr Leu Thr Lys Glu Glu Cys Leu 35 40 45

Lys Lys Cys Ala Thr Val Thr Glu Asn Ala Thr Gly Asp Leu Ala Thr 50 60

Ser Arg Asn Ala Ala Asp Ser Ser Val Pro Ser Ala Pro Arg Arg Gln 65 70 75 80

Asp Ser Glu Asp His Ser Ser Asp Met Phe Asn Tyr Glu Glu Tyr Cys 85 90 95

Thr Ala Asn Ala Val Thr Gly Pro Cys Arg Ala Ser Phe Pro Arg Trp
100 105 110

Tyr Phe Asp Val Glu Arg Asn Ser Cys Asn Asn Phe Ile Tyr Gly Gly 115 120 125

Cys Arg Gly Asn Lys Asn Ser Tyr Arg Ser Glu Glu Ala Cys Met Leu 130 \$135\$

Arg Cys 145

<210> 51

<211> 1530

<212> DNA

<213> Artificial Sequence

<220>

<223> Consensus bikunin sequence of Fig. 4C.

<220>

<221> misc_feature

<222> (46)..(46)

<223> "n" is any nucleotide.

<220>

<221> misc_feature

<222> (117)..(117)

<223> "n" is any nucleotide.

<220>
<221> misc_feature
<222> (313)..(313)
<223> "n" is any nucleotide.

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| ttctgaaaga | aggaaagtaa | aatgtacaag | tttaataaaa | aggggccttc | ccctttagaa | 1500 |
|------------|------------|------------|------------|------------|------------|------|
| taaaaaaaaa | aaaaaaaaa | aaaaaaaaa | | | | 1530 |

<210> 52 <211> 170 <212> PRT <213> Homo sapiens

<400> 52

Ala Asp Arg Glu Arg Ser Ile His Asp Phe Cys Leu Val Ser Lys Val 1 5 10 15

Val Gly Arg Cys Arg Ala Ser Met Pro Arg Trp Trp Tyr Asn Val Thr 20 25 30

Asp Gly Ser Cys Gln Leu Phe Val Tyr Gly Gly Cys Asp Gly Asn Ser 35 40 45

Thr Glu Asn Ala Thr Gly Asp Leu Ala Thr Ser Arg Asn Ala Ala Asp 65 70 75 80

Ser Ser Val Pro Ser Ala Pro Arg Arg Gln Asp Ser Glu Asp His Ser 85 90 95

Ser Asp Met Phe Asn Tyr Glu Glu Tyr Cys Thr Ala Asn Ala Val Thr 100 105 110

Gly Pro Cys Arg Ala Ser Phe Pro Arg Trp Tyr Phe Asp Val Glu Arg 115 120 125

Asn Ser Cys Asn Asn Phe Ile Tyr Gly Gly Cys Arg Gly Asn Lys Asn 130 135 140

Ser Tyr Arg Ser Glu Glu Ala Cys Met Leu Arg Cys Phe Arg Gln Gln 145 150 155 160

Glu Asn Pro Pro Leu Pro Leu Gly Ser Lys 165 170

<210> 53

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<212> PRT
<213> Homo sapiens
<400> 53
Met Ala Gln Leu Cys Gly Leu Arg Arg Ser Arg Ala Phe Leu Ala Leu
Leu Gly Ser Leu Leu Leu Ser Gly Val Leu Ala
<210> 54
<211> 23
<212> PRT
<213> Homo sapiens
<400> 54
Met Leu Arg Ala Glu Ala Asp Gly Val Ser Arg Leu Leu Gly Ser Leu
Leu Leu Ser Gly Val Leu Ala
          20
<210> 55
<211> 102
<212> DNA
<213> Artificial Sequence
<220>
<223> 5' sense oligonucleotide used for construct #2 in Example 5.
<400> 55
60
                                                               102
tgtagagctt cttttccaag atggtacttt gatgttgaaa ga
<210> 56
<211> 129
<212> DNA
<213> Artificial Sequence
<223> 3' antisense oligonucleotide used for construct #2 in Example 5.
<400> 56
actggatcct cattggcgaa aacatctcaa catacaggct tcttcagatc tgtaagaatt
                                                                60
tttattacct ctacaaccac cgtaaataaa attattacaa gaatttcttt caacatcaaa
                                                               120
gtaccatct
                                                               129
```

<211> 27

```
<210> 57
<211> 108
<212> DNA
<213> Artificial Sequence
<223> 5' sense oligonucleotide used for construct #3 in Example 5.
<400> 57
gaaggggtaa gcttggataa aagaaattac gaagaatact gtactgctaa tgctgttact
                                                                     60
ggtccatgta gagcttcttt tccaagatgg tactttgatg ttgaaaga
                                                                    108
<210> 58
<211> 117
<212> DNA
<213> Artificial Sequence
<223> 5' sense oligonucleotide used for construct #4 in Example 5.
<400> 58
gaaggggtaa gcttggataa aagagatatg tttaattacg aagaatactg tactgctaat
                                                                     60
gctgttactg gtccatgtag agcttctttt ccaagatggt actttgatgt tgaaaga
                                                                    117
<210> 59
<211> 19
<212> DNA
<213> Artificial Sequence
<220>
<223> Sense oligonucleotide used in PCR in Example 8.
<400> 59
cacctgatcg cgagacccc
                                                                     19
<210> 60
<211> 23
<212> DNA
<213> Artificial Sequence
<220>
<223> Antisense oligonucleotide used in PCR in Example 8.
<400> 60
ctggcggaag cagcggagca tgc
                                                                     23
<210> 61
<211> 45
<212> DNA
```

```
<213> Artificial Sequence
<220>
<223> Oligonucleotide used in in vitro mutagenesis in Example 9.
                                                                     45
cgcgtctcgg ctgacctggc cctgcagatg gcgcacgtgt gcggg
<210> 62
<211> 60
<212> DNA
<213> Artificial Sequence
<220>
<223> Oligonucleotide used in in vitro mutagenesis in Example 9.
ctgccccttg gctcaaagta ggaagatctt cccccgggg gggtggttct ggcggggctg
                                                                     60
<210> 63
<211> 14
<212> PRT
<213> Homo sapiens
<400> 63
Leu Arg Cys Phe Arg Gln Gln Glu Asn Pro Pro Pro Leu Gly
<210> 64
<211> 20
<212> PRT
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<400> 64
Ala Asp Arg Glu Arg Ser Ile His Asp Phe Cys Leu Val Ser Lys Val
Val Gly Arg Cys
<210> 65
<211> 20
<212> PRT
<213> Homo sapiens
<400> 65
Phe Asn Tyr Glu Glu Tyr Cys Thr Ala Asn Ala Val Thr Gly Pro Cys
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5

Arg Ala Ser Phe 20 <210> 66 <211> 11 <212> PRT <213> Homo sapiens <400> 66 Pro Arg Tyr Val Asp Gly Ser Gln Phe Tyr Gly <210> 67 <211> 55 <212> PRT <213> Homo sapiens <400> 67 Val Val Leu Ala Gly Leu Phe Val Met Val Leu Ile Leu Phe Leu 10 Gly Ala Ser Met Val Tyr Leu Ile Arg Val Ala Arg Arg Asn Gln Glu Arg Ala Leu Arg Thr Val Trp Ser Ser Gly Asp Asp Lys Glu Gln Leu 40 Val Lys Asn Thr Tyr Val Leu 50 <210> 68 <211> 43 <212> PRT <213> Homo sapiens <400> 68 Val Val Leu Ala Gly Leu Phe Val Met Val Leu Ile Leu Phe Leu 5 Gly Ala Ser Met Val Tyr Leu Ile Arg Val Ala Arg Arg Asn Gln Glu 25

Arg Ala Leu Arg Thr Val Trp Ser Phe Gly Asp

<210> 69

<211> 55

<212> PRT

<213> Homo sapiens

<400> 69

Val Val Val Leu Ala Gly Leu Phe Val Met Val Leu Ile Leu Phe Leu
1 5 10 15

Gly Ala Ser Met Val Tyr Leu Ile Arg Val Ala Arg Arg Asn Gln Glu 20 25 30

Arg Ala Leu Arg Thr Val Trp Ser Ser Gly Asp Asp Lys Glu Gln Leu 35 40

Val Lys Asn Thr Tyr Val Leu 50 55

<210> 70

<211> 213

<212> PRT

<213> Homo sapiens

<400> 70

Ala Asp Arg Glu Arg Ser Ile His Asp Phe Cys Leu Val Ser Lys Val 1 5 10 15

Val Gly Arg Cys Arg Ala Ser Met Pro Arg Trp Trp Tyr Asn Val Thr

Asp Gly Ser Cys Gln Leu Phe Val Tyr Gly Gly Cys Asp Gly Asn Ser 35

Asn Asn Tyr Leu Thr Lys Glu Glu Cys Leu Lys Lys Cys Ala Thr Val 50 60

Thr Glu Asn Ala Thr Gly Asp Leu Ala Thr Ser Arg Asn Ala Ala Asp 65 70 75 80

Ser Ser Val Pro Ser Ala Pro Arg Arg Gln Asp Ser Glu Asp His Ser 85 90 95

Ser Asp Met Phe Asn Tyr Glu Glu Tyr Cys Thr Ala Asn Ala Val Thr 100 105 110

Gly Pro Cys Arg Ala Ser Phe Pro Arg Trp Tyr Phe Asp Val Glu Arg 120 115

Asn Ser Cys Asn Asn Phe Ile Tyr Gly Gly Cys Arg Gly Asn Lys Asn 135 130

Ser Tyr Arg Ser Glu Glu Ala Cys Met Leu Arg Cys Phe Arg Gln Gln 155 150 145

Glu Asn Pro Pro Leu Pro Leu Gly Ser Lys Val Val Leu Ala Gly 170 165

Leu Phe Val Met Val Leu Ile Leu Phe Leu Gly Ala Ser Met Val Tyr 185

Leu Ile Arg Val Ala Arg Arg Asn Gln Glu Arg Ala Leu Arg Thr Val 200 195

Trp Ser Phe Gly Asp 210

<210> 71 <211> 225

<212> PRT

<213> Homo sapiens

<400> 71

Ala Asp Arg Glu Arg Ser Ile His Asp Phe Cys Leu Val Ser Lys Val

Val Gly Arg Cys Arg Ala Ser Met Pro Arg Trp Trp Tyr Asn Val Thr 25 20

Asp Gly Ser Cys Gln Leu Phe Val Tyr Gly Gly Cys Asp Gly Asn Ser 40 35

Asn Asn Tyr Leu Thr Lys Glu Glu Cys Leu Lys Lys Cys Ala Thr Val 55 50

Thr Glu Asn Ala Thr Gly Asp Leu Ala Thr Ser Arg Asn Ala Ala Asp 70

Ser Ser Val Pro Ser Ala Pro Arg Arg Gln Asp Ser Glu Asp His Ser 85 90 95

Ser Asp Met Phe Asn Tyr Glu Glu Tyr Cys Thr Ala Asn Ala Val Thr 100 \$105\$ 110

Gly Pro Cys Arg Ala Ser Phe Pro Arg Trp Tyr Phe Asp Val Glu Arg 115 120 125

Asn Ser Cys Asn Asn Phe Ile Tyr Gly Gly Cys Arg Gly Asn Lys Asn 130 135 140

Ser Tyr Arg Ser Glu Glu Ala Cys Met Leu Arg Cys Phe Arg Gln Gln 145 150 155 160

Glu Asn Pro Pro Leu Pro Leu Gly Ser Lys Val Val Leu Ala Gly
165 170 175

Leu Phe Val Met Val Leu Ile Leu Phe Leu Gly Ala Ser Met Val Tyr 180 185 190

Leu Ile Arg Val Ala Arg Arg Asn Gln Glu Arg Ala Leu Arg Thr Val
195 200 205

Trp Ser Ser Gly Asp Asp Lys Glu Gln Leu Val Lys Asn Thr Tyr Val 210 215 220

Leu

225

<210> 72

<211> 19

<212> PRT <213> Homo sapiens

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<223> "Xaa" is Ile, Thr, Asn, or Ser.

<220>

<221> MISC_FEATURE

<222> (11)..(11)

<223> "Xaa" is Val, Ala, Glu, or Gly.

<221> MISC FEATURE

<222> (17)..(17)

<223> "Xaa" is Ser, Pro, Thr, or Ala.

<220>

<221> MISC_FEATURE
<222> (19)..(19)
<223> "Xaa" is Tyr, His, Asn, or Asp.

<400> 72

Arg Pro Leu Gln Arg Tyr Val Ser Xaa Ile Xaa Arg Ile Ile Ala Pro 10

Xaa Thr Xaa

<210> 73 <211> 108 <212> PRT <213> Homo sapiens

<400> 73

Pro Gly His Gln Gln Glu Cys Ser Gly Phe Leu Cys Pro Lys Ser Pro

Arg Arg Gln Asp Ser Glu Asp His Ser Ser Asp Met Phe Asn Tyr Glu

Glu Tyr Cys Thr Ala Asn Ala Val Thr Gly Pro Cys Arg Ala Ser Phe

Pro Arg Trp Tyr Phe Asp Val Glu Arg Asn Ser Cys Asn Asn Phe Ile

Tyr Gly Gly Cys Arg Gly Asn Lys Asn Ser Tyr Arg Ser Glu Glu Ala

Cys Met Leu Arg Cys Phe Arg Gln Gln Glu Asn Pro Pro Leu Pro Leu

Gly Ser Lys Val Val Leu Ala Gly Ala Val Ser 100

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<210> 74
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<212> PRT
<213> Homo sapiens
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<222>
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<223> "Xaa" is Asp or Glu.
<400> 74
Ser Phe Ser Trp Gly Ala Ser Met Val Leu Leu Ile Pro Gly Gly Lys
Glu Glu Pro Gly Ala Cys Pro Ala Xaa Arg Leu Glu Leu Arg Arg
                               25
<210> 75
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<223> "n" is any nucleotide.
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<221> misc_feature
<222> (510)..(510)
<223> "n" is any nucleotide.
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                                                                     60
ccacgggtga cctggccacc agcaggaatg cagcggattc ctctgtccca agtgctccca
                                                                    120
gaaggcagga ttctgaagac cactccagcg atatgttcaa ctatgaagaa tactgcaccg
                                                                    180
ccaacgcagt cactgggcct tgccgtgcat ccttcccacg ctggtacttt gacgtggaga
                                                                    240
ggaactcctg caataacttc atctatggag gctgccgggg caataagaac agctaccgct
                                                                    300
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ctgaggaggc ctgcatgctc cgctgcttcc gccagcagga gaatcctccc ctgccccttg
                                                                      360
gctcaaaggt ggtggttctg gccggggctg tttcgtgatg gtgttgatcc ttttcctggg
                                                                      420
gagentecat ggtettactg atteegggtg geaaggagga accaggageg tgeeetgegg
                                                                      480
ancgtctgga gcttcggaga tgacaagggn t
                                                                      511
<210> 76
<211> 31
<212> PRT
<213> Artificial Sequence
<220>
<223> Amino acids 184-214 of translation of consensus sequence in Fig. 3.
<220>
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<223> "Xaa" is Asp or Glu.
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Ser Phe Ser Trp Gly Ala Ser Met Val Leu Leu Ile Pro Gly Gly Lys
                5
                                    10
Glu Glu Pro Gly Ala Cys Pro Ala Xaa Arg Leu Glu Leu Arg Arg
            20
                                25
<210> 77
<211> 312
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<223> "n" is any nucleotide.
<400> 77
qcqacctccq cqcqttqqqa ggtgtaqcqc ggctctgaac gcgtngagng gccgttgagt
                                                                     60
gtcgcaggcg gcgagggcgc gagtgaggag cagacccagg catcgcgcgc cgagaagncg
                                                                    120
ggcgtcccca cactgaaggt ccggaaaggc gacttccggg ggctttggca cctggcggac
                                                                    180
cctcccggag cgtcggcacc tgaacgcgag gcgctccatt gcgcgtgcgt ntgaggggct
                                                                    240
tecegeacet gategegaga ecceaacgge tggtggegte geetgegegt eteggetgag
                                                                    300
                                                                     312
ctggncatgt cg
<210> 78
<211> 330
<212> DNA
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<223> "n" is any nucleotide.
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<222> (321)..(321)
<223> "n" is any nucleotide.
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gcgacctccg cgcgttggga ggtgtagcgc ggctctgaac gcgtgcaggg ccgttgagtg
                                                                     60
tegeaggegg egagggegeg agtgaggage agacceagge ategegegee gagaagnegg
                                                                     120
                                                                     180
gentecceae actgaaggte eggaaaggeg actteegggg getttggeae etggeggaee
ctcccggagc gtggcacctg aacgcgaggc gctccattgc gcgtgcgttt gaggggcttc
                                                                     240
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330
ggccatggcg cactgtgcgg ngctgaggcg
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<223> "n" is any nucleotide.
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                                                                     60
aaggccgggc gtccccacac tgaaggtccg gaaaggcgac ttccgggggc tttggcacct
                                                                    120
ggcggaccet cccggagcgt cggcacctga acgcgaggcg ctccattgcg cgtgcgtttg
                                                                    180
aggggettee egeacetgat egegagaeee caaeggetgg tngegteget negegteteg
                                                                    240
                                                                    283
gctgagcttg gccatggcgc antgttncgg gctnaggcgg acg
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ccgcacctga tcgcgagacc ccaacggctg gtggcgtcgc ctgcgcgtct cggctgagct

300

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                                                                                60
                                                                               120
cgcaggcggc agggcngagt gaggagcaga cccaggcatc gcgcgccgag aagncgggcg
tecceacact gaaggteegg aaaggegact teeggggget ttggeacetg geggaegtee
                                                                               180
cggagcnggc acctgaacgc gaggcgctcc attgcgcgtg cgtttgaggg gcttcccgca
                                                                               240
cctgatcgcg agaccccaac ggctggtngc gtcgctggcg cgttctcggc tgagctggcc
                                                                               300
atggcgcant gttgcgngct gaggcggacc gncgtttttc ttcgccttgc tgggattcgc
                                                                               360
ttgcttcctn tctgggggtt cctgggcggc cgaccgagaa cgcagcatcc aagaattttt
                                                                               420
                                                                               423
gcc
<210> 81
<211> 344
<212> DNA
<213> Homo sapiens
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<222> (313)..(313)
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ggaggagcag acccaggcat cgcgcgccga gaagncgggc gtccccacac tgaaggtccg
gaaaggcgac ttccgggggc tttggcacct ggcggaccct cccggagcgt cggcacctga
                                                                        120
acgcgaggcg ctccattgcg cgtgcgtntg gaggggcttc ccgcacctga tcgcgagacc
                                                                        180
ccaacggctg gtgggcgtcg ctgcgcgtct tcggctgagc tgggccatgg cgcanttgtt
                                                                        240
gegggetgag geggaegegg negtttttte gneettgetg ggattegttg ttnetetetn
                                                                        300
                                                                        344
ggggttctgg ggnggccgan cgagaacgca agcattcacg attt
<210> 82
<211> 253
<212> DNA
<213> Homo sapiens
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<222> (159)..(159)
<223> "n" is any nucleotide.
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<222> (233)..(233)
<223> "n" is any nucleotide.
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                                                                            60
getteeegea eetgategeg agaccecaac ggetggtgge gtegetgege gteteggetg
                                                                           120
agetggccat ggegcantgt tgegngetga ggeggeggne gttttetege etgetgggat
                                                                           180
cqctqctcct ctctggggtc ctggcggccg accgagaacg cagcatccac ganttcttcc
                                                                           240
                                                                           253
tggtgttcga agg
<210> 83
<211> 419
<212> DNA
<213> Homo sapiens
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<222> (313)..(315)
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                                                                         60
tgaggagcag acccaggcat cgcgcgccga gaagncgggc gtccccacac tgaaggtccg
                                                                        120
gaaaggcgac ttccgggggc tttggcacct ggcggaccct cccggagcgt cggcacctga
                                                                        180
acgcgaggcg ctccattgcg cgtgcgtttg aggggcttcc cgcacctgat cgcgagaccc
                                                                        240
caacggctgg tggcgtcgcc tgcgcgtctc ggctgagctg gccatggcgc antggtgcgg
                                                                        300
gcttgaggcg gannngccgt ttctcgcctg ctgggatcgc tgctcctctc tggggtcctg
                                                                        360
gcggccgacc gagaacgcag catccacgac ttctgcctgg tgtcgaaggt ggtgggcag
                                                                        419
<210> 84
<211> 477
<212> DNA
<213> Homo sapiens
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<222> (223)..(223)
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<222> (232)..(232)
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 <222> (328)..(328)
<223> "n" is any nucleotide.
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  <222> (405)..(405)
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<222> (437)..(437)
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<222> (449)..(449)
<223> "n" is any nucleotide.
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<221> misc_feature
<222> (458)..(458)
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agacccaggc atcgcgccc gagaagncgg gcgtccccac actgaaggtc cggaaaggcg
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acttccgggg gctttggcac ctggcggacc ctcccggagc gtcggcacct gaacgcgagg
                                                                    120
cctccattgc cgtgcgttng aggggcttcc cggaacttga tcgcgagacc ccaacggctg
gtggcgtcgc tgcgcgtcct cggctgagct ggccatggcg cantggtgcc gngctgaggc
cggagggccg gtttctcgcc ttgctgggat cgctgctcct ctctggggtc ctggcggccg
                                                                    300
ancgaagaan gcagcaatcc angaattnct gcctggtgtt cgaaagttgg tgggcanatt
                                                                    360
ccggggcctt catgnctaag gttggttggt anaatgtnaa ttaangattc ttgcaactgt
                                                                    477
ttgtgtnatt ggggctntta aacggaaana caataatnac ctgaccaaag aagnaat
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accgagaacg cagcatccac gacttctgcc tggtgtcgaa ggtggtgggc agattccggg
                                                                           120
cctccatgcc taggtggtgg tacaatgtca ctgacggatc ctgccagctg tttgtgtatg
                                                                           180
ggggctgtga cggaaacagc aataattacc tgaccaagga ggagtgcctc aagaaatgtg
                                                                           240
ccactgtcac agagaatgcc acgggtgacc tggccaccag caggaatgca gcggattcct
                                                                           300
                                                                           360
ctgtcccaag tgctcccaga aggcaggatt cttgaagacc acttcagcga tatgtttcaa
                                                                           393
ntattgnaag aataattgca ccgncaacgn att
<210> 86
<211> 428
<212> DNA
<213> Homo sapiens
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<222> (48)..(48)
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<222> (425)..(425)
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                                                                          60
agaacgcagc atccacgact tctgcctggt gtcgaaggtg gtgggcagat gccgggcctc
                                                                         120
catgcctagg tggtggtaca atgtcactga cggatcctgc cagctgtttg tgtatggggg
                                                                         180
ctgtgacgga aacagcaata attacctgac caaggaggag tgcctcaaga aatgtgccac
                                                                         240
tgtcacagag aatgccacgg gtgacctggc caccagcagg aatgcagcgg attcctctgt
                                                                         300
cccaagtgct cccagaaggc aggattctga agaccactcc agcgatatgt tcaactatga
                                                                         360
agaatactgg caccgccaac gcattcactg ggcctgcgtg catccttccc acgctggtac
                                                                         420
                                                                         428
tttgncgt
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<212> DNA
<213> Homo sapiens
<220>
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<222> (7)..(7)
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<222> (403)..(403)
<223> "n" is any nucleotide.
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<222> (409)..(409)
<223> "n" is any nucleotide.
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ctggganteg ctgctcctct ctggggtcct ggcggccgac cgagaacgca gcatccacga
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120

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                                                                    180
                                                                    240
taattacctg accaaggagg agtgcctcaa gaaatgtgcc actgtcacag agaatgccac
gggtgacctg gccaccagca ggaatgcagc ggattcctct gtcccaagtg ctcccagaag
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gcaggattct gaagaccact ccagcgatat gttcaactat gaagaatact gcaccgccaa
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| ctctgtccca agtgctccca gaaggcagga ttctgaagac cactccagcg atatgttcaa | 180 |
| ctatgaagaa tactgcaccg ccaacgcagt ncactgggcc ttgcgtggca tnccttccca | 240 |
| cgctngtact ttgacgtgga gaggaactcc tggcaataac ttcatctatg gaggcttgcc | 300 |
| ggggcaatna agaacagntt accgctcttt aggaggcctg cat | 343 |
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| ccacgggtga cctggccacc agcaggaatg cagcggattc ctctgtccca agtctcccag | 120 |
| aaggcaggat totgaagaco actocagoga tatgttcaac tatgaagaat actgcacogo | 180 |
| caacgcagtc actgggcctt gccgtgcatc cttcccacgc tggtactttg acgtggagag | 240 |
| gaactcotgc aataacttca totatggagg otgooggggc aataagaaca getaccgotc | 300 |
| tgaggaggcc tgcatgctcc gctgcttccg ccagcaggag aatcctcccc tgccccttgg | 360 |
| ctcaaaggtg gtggttctgg ccggggctgt ttcgtgatgg tgttgatcct tttcctgggg | 420 |
| | |
| agentecatg gtettactga tteegggtgg caaggaggaa ecaggagegt geeetgegga | 480 |

| ncgtctggag cttcggagat gacaagggnt | 510 |
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| tcctggggag cctccatggt ctacctgatc cgggtggcac ggagggaacc agggagcgtg | 180 |
| ccctgcgcac cgtctgggag ctccggagat gacaagggag cagctgggtg aagaacacat | 240 |
| atgtteetgt tgacegneet gttegecaag aggattgggg gaagggaggg gga | 293 |
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| <220> <221> misc_feature <222> (147)(147) <223> "n" is any nucleotide. | |
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| gggctgttcg tgatggtgtt gatccctcct tcccgggagc ctcccatggt cctaccctga | 120 |
| teegggtgge aeggaggaae eeagganegt geeetgegea eegtetggag eteeggagat | 180 |
| gacaaggagc agctggtgaa gaacacatat gtcctgtgac cgccctgtcg ccaagaggac | 240 |
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                                                                      120
gagaatcete ceetgeeect tggeteaaag gtggtggtte tggegggget gttegtgatg
                                                                      180
gtgttgatcc tcttcctggg agcctccatg gtntacctga tccgggtngc acggaggaac
                                                                      240
cagggagcgt gccctgcgna ccgtctngga gctccggaga tgacaaggag cagctggtga
                                                                      300
agaacacata tgtcctgtga ccgncctgtt cgncaagagg actnggggaa aggggagggg
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tggcggggct gttcgtgatg gtgttgatcc tcttcctggg agcctccatg gtctacctga
                                                                          180
tccgggtggc acggaggaac cagggagcgt gccctgcgca ccgtctggga gctccggaga
                                                                          240
tgacaaggga gcagctggtg aagaacacat atgttcctgt tgaccgccct gttcgccaag
                                                                          300
agggantggg ggaaggggag ggggaganta ttgttgttga gnttttttt aaaattagga
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ggggnttgan ttcgggnttt tnagttgatc catttagggg gntgag
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aaaggtggtg gttctggcgg ggctgttcgt gatggtgttg atcctcttcc tgggagcctc
                                                                    120
                                                                    180
catggtctac ctgatccggg tngcacggag gaaccaggag cgtgccctgc gcaccgtctg
gagctccgga gatgacaagg agcagctggt gaagaacaca tatgtcctgt gaccgccctg
                                                                    240
tcgccaagag gactggggaa gggaggggag actatgtgtg agctttttt aaatagaggg
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gggtggcacg gaggaaccag gagcgtgccc tgcgcaccgt ctggagctcc ggagatgaca
                                                                    120
                                                                    180
aggagcagct ggtgaagaac acatatgtcc tgtgaccgcc ctgtcgccaa gaggactggg
gaagggaggg gagactatgt gtgagctttt tttaaataga gggattgact cggatttgag
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tgatcattag ggctgaggtc tgtttctctg ggaggtagga cggctgcttc ctgggtcttg
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gcagggatgg ggtttgcttt gggaaatcct cttnggaggc tcctccttcg catgggcctt
                                                                    360
gcagtetngg cagcanecee egagtttttt teettegetg atcegattte tttteeteea
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ggtaagaatt tttctttt
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                                                                    120
gagactatgt gtgagctttt tttaaataga gggattgact cggatttgag tgatcattag
                                                                    180
ggctgaggtc tgtttctctg ggaggtagga cggctgcttc ctggtctggc agggatgggt
                                                                    240
ttgctttgga gaatcctcta ngaggetect cetegeatgg cetgeagtet ggeageagee
                                                                    300
ccgagttgtt tcctcgctga tcgatttctt tcctccaggt agagttttct ttgcttatgt
                                                                    360
tgaattccat tgcctctttt ctcatcacag aagtgatgtt ggaatcgttt cttttgtttt
                                                                    420
gtctgattta tgggtttttt ttaagtat
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                                                                         120
cageccegag ttgttteete getgategat ttettteete caggtagagt tttetttget
                                                                         180
tatgttgaat tocattgcct cttttctcat cacagaagtg atgttggaat cgtttctttt
                                                                         240
gtttgtctga tttatggttt ttttaagtat aaacaaaagt tttttattag cattctgaaa
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                                                                         331
gaaggaaagt aaaatgtaca agtttaataa a
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                                                                    120
ttctttgctt atgttgaatt ccattgcctc ttttctcatc acagaagtga tgttggaatc
                                                                    180
gtttcttttg tttgtctgat ttatggtttt tttaagtata aacaaaagtt ttttattagc
                                                                    240
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aatnaaaana aaaaagggtg
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tegeatggcc tgcagtetgc agcageeceg agttgtttec tegetgateg atttetttec
                                                                    180
tccaggtaga gttttctttg cttatgttga attccattgc ctcttttctc atcacagaag
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tgatgttgga atcgtttctt ttgtttgtct gatttatggt ttttttaagt ataaacaaaa
                                                                    300
gttttttatt agcattctga aagaaggaaa gtaaaatgta caagtttaat aaaaaggggc
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cncatcacag aagtgatgtt ggaatcgttt cttttgtttg tctgatttat ggttttttta
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                                                                 120
attccattgc ctcttttctc atcacagaag tgatgttgga atcgtttctt ttgtttgtct
                                                                 180
gatttatggt ttttttaagt ataaacaaaa gttttttatt agcattctga aagaaggaaa
                                                                 240
gtaaaatgta caagtttaat aaaaaggggc cttccccttt agaataaatt tcagcatgtg
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ctttcaaaaa a
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tagagttttc ctttgnctta tgttgaattc cattgcctct tttactcatc acagaagtga
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tgttggaatc gtttcttttg tttgtctgat ttatggtttt tttaagtata aacaaaagtt
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| gcatggcctg | cagtctggca | gcagccccga | gttgtttcct | cgctgancga | tttctttcct | 120 |
| ccaggtagag | ttttctttgc | ttatgttgaa | ttccattgcc | tcttttctca | tcacagaagt | 180 |
| gatgttggaa | tcgtttcttt | tgtttgtctg | atttatggtt | tttttaagta | taaacaaaag | 240 |
| ttttttatta | gcattctgaa | agaaggaaag | taaaatgtac | aagtttaata | aaaaggggcc | 300 |
| ttccccttta | gaataaaaaa | aaaaaaaaa | aaaaaaaaa | aaa | | 343 |